FORM PTO-1390 (REV. 12-2001) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: SDF-02-8

U S APPLICATION NO (If known, see 37 CFR 1 5): 10/069780

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/JP00/05677	August 24, 2000	September 3, 1999

TITLE OF INVENTION: Medicinal Compositions for Oral Use

APPLICANT(S) FOR DO/EO/US: Yoshio OKUBO, Hidetaka MORIYA, Noriyasu SAITO, Hiroshi YUASA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [X] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [X] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter 2 and 35 U.S.C. 1 821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [ ] Other items or information:

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
10/069780	PCT/JP00/05677	SDF-02-8

21. [X] The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	8 - 20 =	0	x **$18.00**	$
Independent claims	2 - 3 =	0	x **$84.00**	$
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$

TOTAL OF ABOVE CALCULATIONS =	$ 890.00	
[ ] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$	
SUBTOTAL =	$ 890.00	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$	
TOTAL NATIONAL FEE =	$	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$	
TOTAL FEES ENCLOSED =	$ 890.00	
	Amount to be refunded:	$
	charged:	$

a. [X] A check in the amount of $ 890.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [ ] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed.

d. [ ] Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

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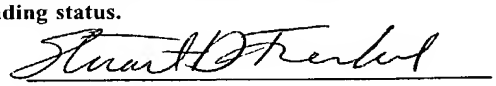

SIGNATURE

Stuart D. Frenkel

NAME

29,500

REGISTRATION NUMBER

DESCRIPTION

MEDICINAL COMPOSITIONS FOR ORAL USE

Technical Field

The present invention relates to an oral medicinal composition preferable for administration to patients with difficulty in swallowing, such as patients with deglutition disorder, aged persons, children or patients needing rest due to post-surgery, and a method for administering the oral medicinal composition.

Background of the Invention

Previously, solid dosage forms such as capsules, tablets, granules and powders as well as liquid dosage forms such as liquids for internal use, suspensions, emulsions, syrups, elixirs, aromatic waters and lemonades, have been generally used as oral pharmaceutical dosage forms. However, not any foamed dosage forms have been used for oral use yet.

As foamed dosage forms, alternatively, foamed aerosols have been commonly used for cosmetic products and external preparations. However, such foamed dosage forms have been never used as oral pharmaceutical dosage forms. Additionally, for the route of administration into oral cavity or throat, powders, liquids for internal use, suspensions and the like have been partly administered by modifying them into aerosols or into

the form of fog or drop by using an appropriate device. Nevertheless, not any method for modifying them into foam for oral administration has been used yet.

When patients with difficulty in swallowing or not good at swallowing, such as patients with deglutition disorder, aged persons, children or patients needing rest due to post-surgery, intend to take oral pharmaceutical dosage forms of the related art, the patients have encountered various problems during administration, because solid dosage forms such as general capsules, tablets, granules and powders per se involve difficulty in swallowing and therefore require water during dosing and because these dosage forms should instantaneously be poured along with water into throat, which sometimes causes an episode of choking.

In case of allowing patients lying on their side in bed, such as patients needing rest due to post-surgery and the like and bedridden patients, to take such solid dosage forms, it is difficult for the patients to swallow the dosage forms per se. Further, these solid dosage forms are readily incorporated into airway, which induces additional pain.

Still further, patients at the last stage of cancer and patients with severe oral herpes simplex complain unendurable pain in contact to liquids, to say nothing of solids. Therefore, serious disadvantages have been induced in their daily life.

Insofar, dosage forms of orally disintegrating type have

been developed, which can be administered with a small volume of water and are suitable for persons with swallowing difficulty including patients with deglutition disorder or aged persons. However, all of the dosage forms are solid dosage forms, so the dosage forms quite differ from the foamed dosage form of the invention.

Meanwhile, even relatively readily incorporable liquid dosage forms such as liquids for internal use, suspensions, emulsions, syrups, elixirs, aromatic waters and lemonades may happen to be rapidly poured into throat, so the liquid dosage forms are also readily incorporated into airway, like solid dosage forms to be poured along with water. Thus, such liquid dosage forms may occasionally be never incorporated, because of an episode of choking.

As described above, additionally, even liquid contact causes strong physical irritation, so such liquid dosage forms are not satisfactorily sufficient for patients at the last stage of cancer or patients with severe oral herpes simplex, with complaints of unendurable pain.

In case of liquid dosage forms, further, the liquid dosage forms should be measured at the cost of complicated labor before administration. Additionally, the measurement of a dose in a constant manner has not been so simple, disadvantageously.

In case that the liquid dosage forms of the related art should be applied at a topical site, such as throat, further,

the liquid dosage forms can rapidly reach a site where the pharmaceutical component therein can be absorbed or a site to be therapeutically treated, but the liquid dosage forms also rapidly pass through such site, disadvantageously, with no possibility of sufficient therapeutic effects.

Disclosure of the Invention

The invention relates to an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is ejected from a foam-developing device to be prepared into foam.

Additionally, the invention relates to a method for administering an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is ejected from a foam-developing device to prepare them into foam for administration.

Best Mode for Carrying out the Invention

A problem of the invention is to develop a dosage form administrable to patients at the last stage of cancer and patients with severe oral herpes simplex, which can be dosed with no need of water and can be readily swallowed but be never rapidly poured into throat, involving less chance of incorporation into airway and no occurrence of choking, and which causes less physical irritation, and a method for

administrating such dosage form.

Further, a problem of the invention is to develop a dosage form which can be dosed routinely at a constant amount with no need of complicated measurement and which can be readily incorporated by persons lying on their side in bed and can be retained sufficiently at a site in oral cavity or throat where the pharmaceutical component therein can be absorbed or a site to be therapeutically treated, and a method for administrating such dosage form.

The present inventors have made intensive investigations so as to develop an oral medicinal composition which can overcome the problem and which is suitable for dosing to patients with deglutition disorder or persons with swallowing difficulty, and a method for administering such oral medicinal composition. Consequently, the inventors have found that by preparing oral liquid dosage forms such as liquids for internal use, suspensions, emulsions, syrups, elixirs, aromatic waters and lemonades into foam for administration, to allow the resulting foam to again resume the liquid forms after administration, the oral liquid dosage forms can be dosed with no water, be readily swallowed with no rapid pouring into throat or not any subsequent incorporation into airway causing an episode of choking, has less physical irritation and can be dosed readily in a safe manner. Thus, the invention has been achieved.

More specifically, the inventors have found that by

modifying an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is turned into foam when ejected form a foam-developing device, into foam via release of the oral medicinal composition from an appropriate foam-developing device and then administering the resulting foam from the foam-developing device, the oral medicinal composition never causes any irritation at the time of dosing, or never requires the supply of extra water or specific effort for swallowing. Further, the oral medicinal composition can be spontaneously poured into throat without rapid influx into throat or without influx into airway which induces choking and is extremely suitable for administration to patients with deglutition disorder or persons with swallowing difficulty.

By measuring a given amount of the medicinal composition into a foam-developing device to allow the medicinal composition to be prepared into foam for administration, additionally, no complicated measurement is required before dosing and a constant dose can be given routinely.

Characteristically, the oral medicinal composition of the invention comprises an active ingredient and at least one foaming agent and is prepared into foam when ejected from a foam-developing device. By foaming the oral medicinal composition prior to administration and then gradually allowing the foamed composition to resume the initial liquid form, the oral medicinal composition can be extremely readily

administered with no irritation during administration, without any water supply, with no chance of choking episode due to the incorporation of the oral medicinal composition or water into airway during dosing, and with no complicated measurement prior to dosing, and the oral medicinal composition can be routinely dosed readily at a constant dose. Thus, the oral medicinal composition exerts innovative effects.

Any foaming agent may be used for the oral medicinal composition of the invention, provided that the foaming agent can prepare non-irritable foam, never occurring interactions such as incompatible combination with the active ingredient and pharmaceutical additives to be contained therein, being endurable of long-term storage and being appropriately self-sustainable when ejected from a foam-developing device. The foaming agents include, for example, polyethylene glycol, stearyl alcohol, saponin, propylene glycol, medium-chain fatty acid triglyceride, cacao butter, sucrose esters of fatty acids, polyoxyl stearate, polyoxyethylene hydrogenated castor oil, polyoxyethylene polyoxypropylene glycol, sorbitan sesquioleate, sorbitan trioleate, sorbitan monolaurate, polysorbate, glyceryl monostearate, sodium lauryl sulfate, lauromacrogol and the like.

Among these foaming agents, polysorbate, polyethylene glycol, and sodium lauryl sulfate are preferably illustrated. A mixture of polyethylene glycol with polysorbate or sodium

lauryl sulfate is particularly preferable.

These foaming agents may be added singly or in a combination of such plural foaming agents. The blend quantity is appropriately determined depending on the physico-chemical properties of the active ingredient and pharmaceutical additives contained therein and the properties of the foaming agent. Approximately, the foaming agent may be satisfactorily blended within a range of 1 to 20 % by weight to the whole oral medicinal composition.

Further, the properties of the resulting foam vary depending on the type of a foaming agent to be added. For example, when polyethylene glycol is used, the duration of the resulting self-sustainable foam is short. Also, when polysorbate and sodium lauryl sulfate are used, the duration of the resulting self-sustainable foam is long. Resulting self-sustainable foam is influenced by the mean molecular weight of foaming agent. By preparing a combination of plural foaming agents by utilizing such properties and further modifying the blend ratio or blend quantities, the duration of the resulting self-sustainable foam can be adjusted depending on the applicable drug or the subject patient.

In case that the oral medicinal composition of the invention is to be applied as a routine pharmaceutical agent for internal use, self-sustainable foam of a relatively shorter duration can be liquefied more rapidly to be then poured through

throat. Therefore, such foam is preferable because the time required for incorporation is shorter. Preferably, the duration of self-sustainable foam is specifically about several seconds to several tens seconds.

In case that the oral medicinal composition is to be applied into oral cavity or throat, self-sustainable foam of a longer duration or a liquid with a higher viscosity has a longer retention time at a site where the pharmaceutical component therein can be absorbed or a site to be therapeutically treated. Thus, such foam or such liquid is preferable because sufficient therapeutic effects can be exerted. In particular, in case that the oral medicinal composition is to be applied into oral cavity, the composition is preferably retained in the oral cavity at a still foaming state. Also, in case that the oral medicinal composition is to be applied into throat, the composition is preferably poured into throat while the composition still retains the foamy state.

As described above, the duration of self-sustainable foam can be adjusted by selecting a foaming agent or preparing a combination of such foaming agents. For preparing an oral medicinal composition with a longer duration of self-sustainable foam, it can be achieved by adding an appropriate viscous agent other than a foaming agent to permit the duration of self-sustainable foam to be longer.

Such viscous agents include, for example, acrylic resin

alkanol amine solution, sodium alginate, propylene glycol alginate, carmellose sodium, xanthan gum, guar gum, glycerin, sodium chondroitin sulfate, purified lanolin, gelatin, dextrin, potato starch, hydroxyethylcellulose, hydroxyethylmethyl-cellulose, hydroxypropylcellulose, hydroxypropylmethyl-cellulose, polyvinylpyrrolidone, strach syrup, yellow beeswax, methylcellulose and the like.

The viscous agent can prolong the duration of self-sustainable foam and raise the viscosity of the resulting liquid, simultaneously, leading to the prolongation of the retention time after liquefaction. Thus, such viscous agent can be also used for the purpose of the local prolongation of the retention time after liquefaction.

These viscous agents can be added singly or in combination of such plural viscous agents. Additionally, the blend quantity is appropriately determined depending on the physico-chemical properties of the active ingredient and pharmaceutical additives to be contained in the initial oral pharmaceutical liquid dosage form and the properties of the viscous agents. Approximately, the blend quantity may be satisfactorily within a range of 1 to 10 % by weight to the whole oral medicinal composition.

The duration of self-sustainable foam varies depending on not only the kind, blend ratio and molecular weight of a foaming agent but also the kinds and amounts of various

pharmaceutical additives such as sweeteners, aromatics, pH adjusting agents, buffering agents and stabilizers, which are appropriately added in a dependent manner on the kind of the solution and in terms of pharmaceutical preparation. Thus, the duration of self-sustainable foam should be essentially adjusted depending on the final formulation.

For preparing the oral medicinal composition of the invention, a foaming agent and, if necessary, a viscous agent are added together with the active ingredient and pharmaceutical additives according to general preparation methods. Otherwise, a routine oral pharmaceutical liquid dosage form is once prepared, to which a foaming agent and, if necessary, a viscous agent are added at the time of administration. In case that the active ingredient to be used is unstable when prepared into a liquid dosage form, satisfactorily, the liquid base without containing the active ingredient for the oral medicinal composition may be preliminarily prepared, to which the active ingredient is then added at the time of administration. Otherwise, the oral medicinal composition may be satisfactorily prepared into powders, such as freeze-dry powders, to which water is added at the time of administration to prepare the oral medicinal composition into liquids.

If necessary, additionally, corrigents or aromatics for use in general formulations may be satisfactorily added. Still

further, pH adjusting agents, buffering agents, stabilizers and the like to keep the solubility and stability may be satisfactorily added depending on the characteristic of the active ingredient.

So as to administer practically the oral medicinal composition of the invention, an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is prepared by a general method and can be turned into foam when ejected from a foam-developing device, is dosed by means of an appropriate foam-developing device; otherwise, a foaming agent and, if necessary, a viscous agent are added to a general oral pharmaceutical liquid dosage form preliminarily prepared, which is then dosed by means of the foam-developing device. In case that the active ingredient is unstable when prepared into a liquid dosage form, a liquid base without containing the active ingredient for an oral medicinal composition is preliminarily prepared, to which the active ingredient is then added at the time of administration. The resulting formulation may be satisfactorily dosed by means of the foam-developing device.

Through the administration by means of a foam-developing device as described above, any complicated procedure for measuring the dose as in the case of dosing general oral pharmaceutical liquid dosage forms can be saved; additionally, a constant volume can be taken consistently; and dosing can be

done in a very easy and safe manner.

The foam-developing device for use in the administration of the oral medicinal composition of the invention may be any foam-developing device with a function to permit the preparation of a given amount of the oral medicinal composition into foam, with no specific limitation. Preferable such foam-developing devices include an aerosol container with a quantitative dosing valve or a container for mixing a given amount of air with a given amount of composition and releasing then the resulting mixture through porous materials such as mesh.

The oral medicinal composition of the invention is applicable to any active ingredient, which can be dissolved, emulsified or suspended in water and can be adjusted of its viscosity on a needed basis.

The oral medicinal composition is preferably applicable to pharmaceutical agents for subject patients with swallowing difficulty or with pain during swallowing, such as patients with deglutition disorder, aged persons, children or patients needing rest due to post-surgery, particularly, pharmaceutical agents such as topical anesthesia for subject patients at the last stage of cancer or patients with severe oral herpes simplex, or pharmaceutical agents to be essentially dosed without water, dosage forms for patients under water intake control, pharmaceutical agents for one draft, and the like. Further,

pharmaceutical agents with relatively less doses are preferable. In case that a large dose is required, the dose can be administered in a dividend manner.

Examples

The contents of the invention will be illustrated in more detail by way of the following Examples and Reference Examples. However, the invention is not limited to the contents.

Example 1

Using sodium lauryl sulfate and polyethylene glycol (Macrogol 6000) as foaming agents, liquids with variable blend ratios were prepared. Distilled water was used as a control. Under observation of foaming, the duration of the resulting self-sustainable foam vs. the change of the blend ratio was measured. For test solutions, sodium lauryl sulfate was blended to the individual ratios in Table 1 below, provided that the concentration of polyethylene glycol was fixed to 10 mg/mL, which was defined as 100. The duration of self-sustainable foam was measured according to the following method (hereinafter referred to as Method A). After ejecting a liquid from a foam-developing device to allow foam to be ejected onto a 30cm height position of a plastic plate in vertical position, the time (second) required for the foam to be subsequently liquefied and flow down until the top of the liquid reached the lower end

of the plate was measured, which was designated the duration of self-sustainable foam. The test was repeated three times. The mean was determined. The results measured are shown below in Table 1. Distilled water (control) never made any foam. The duration of self-sustainable foam was prolonged with increasing the amount of sodium lauryl sulfate.

[Table 1]

	Control (distilled water)	Formulation 1	Formulation 2	Formulation 3
Sodium lauryl sulfate	0	0	0.05	0.5
Macrogol 6000	0	100	100	100
Duration of self-sustainable foam (second)	-	9	53	84

Example 2

Using polysorbate 80 and polyethylene glycol (Macrogol 6000) as foaming agents, liquids with variable blend ratios were prepared. As in Example 1, the duration of the resulting self-sustainable foam vs. the change of the blend ratio was measured under observation of foaming. For test solutions, polysorbate 80 was blended to the individual ratios in Table 2 below, provided that the concentration of polyethylene glycol was fixed to 10 mg/mL, which was defined as 100. The duration of self-sustainable foam was measured by the Method A as in Example 1. The test was repeated three times. The mean was determined. The results measured are shown below in Table 2. The duration of self-sustainable foam was prolonged with

increasing the amount of polysorbate 80.

[Table 2]

	Formulation 1	Formulation 4	Formulation 5
Polysorbate 80	0	5	20
Macrogol 6000	100	100	100
Duration of self-sustainable foam (second)	9	31	41

Example 3

Using sodium lauryl sulfate and polyethylene glycol (Macrogol 6000) as foaming agents as in Example 1, liquids with variable blend ratios between sodium lauryl sulfate and Macrogol 6000 were prepared. The duration of the resulting self-sustainable foam vs. the change of the blend ratio was measured under observation of foaming. For test solutions, the total of sodium lauryl sulfate and Macrogol 6000 was adjusted to 0.5 w/w %. For the purpose of measuring the flow through oral cavity and throat, the duration of self-sustainable foam was measured according to the following method (hereinafter referred to as Method B). After measuring 10 mL of a liquid and ejecting the total volume from a foam-developing device to make the foam on a funnel in connection to a measuring cylinder, the time (second) required for the foam to flow down the funnel to move into the measuring cylinder until 50 % of the foam was liquefied (a liquid volume of 5 mL) was measured, which was designated the duration of self-sustainable foam. The test was

repeated three times. The mean was determined. The results measured are shown below in Table 3. In case of sodium lauryl sulfate alone (Formulation 9), the duration of self-sustainable foam was prolonged and was about 10-fold that of the duration in case of Macrogol 6000 alone (Formulation 6), and the duration of self-sustainable foam was prolonged with increasing the amount of sodium lauryl sulfate.

[Table 3]

	Formulation 6	Formulation 7	Formulation 8	Formulation 9
Sodium lauryl sulfate	0	10	50	100
Macrogol 6000	100	90	50	0
Duration of self-sustainable foam (second)	23	143	199	256

Example 4

Using sodium lauryl sulfate and polyethylene glycol (Macrogol 6000) as foaming agents as in Example 1, liquids were prepared so that the total of the two foaming agents might be 10 mg/mL. For preparing liquids, distilled water was used for one formulation (Formulation 10), while McIlvaine's buffer solution, pH 7 was used for the other formulation (Formulation 11). The duration of self-sustainable foam was measured by absolutely the same method as in Example 1. As the results are shown below in Table 4, the duration of self-sustainable foam was shortened in case of using the buffer solution.

[Table 4]

	Formulation 10	Formulation 11
Preparative solution	distilled water	McIlvaine's buffer solution, pH 7
Sodium lauryl sulfate	0.5	0.5
Macrogol 6000	99.5	99.5
Duration of self-sustainable foam (second)	85	13

Reference Example 1

Stability test

The liquid of the Formulation 11 as prepared in Example 4 was stored in a glass container at 5 °C, 40 °C and 60 °C for 2 weeks. Then, the appearance of the liquid was observed, while the change of the duration of self-sustainable foam was measured. The duration of self-sustainable foam was measured by the Method A of Example 1 and the Method B of Example 3. As shown in the results below in Table 5, the liquid was stable with no significant change of the appearance or the duration of self-sustainable foam.

[Table 5]

Storage conditions	Time of preparation	5 °C	40 °C	60 °C
Appearance	colorless, transparent	colorless, transparent	colorless, transparent	colorless, transparent
Duration of self-sustainable foam as measured by Method A (second)	13	14	15	13
Duration of self-sustainable foam as measured by Method B (in second)	56	56	66	64

Reference Example 2

Dose uniformity test

Adding an active ingredient to the liquid of the Formulation 11 of Example 4 for adjustment to the concentration of 1.25 mg/mL and continuously ejecting the resulting mixture from a foam-developing device (at an ejection volume of 0.8 mL/one time) 10 times for foaming, the content of the active ingredient in the individuals was measured. As the results are shown below in Table 6, the content of active ingredient was almost constant.

[Table 6]

n	1	2	3	4	5	6	7	8	9	10
Content (mg)	0.93	0.95	0.92	0.94	0.94	1.02	0.98	0.99	0.97	0.97

Mean content: 0.96 mg

RSD: 3.2 %

Industrial Applicability

The medicinal composition of the invention can be dosed even to patients at the last stage of cancer and patients with severe oral herpes simplex, because the composition can be dosed without water and easily swallowed with no rapid flow into throat involving less concern of incorporation into airway or no occurrence of choking and because the composition induces less physical irritation. Additionally, the medicinal composition

of the invention can be dosed at a constant amount, involving no complicated measuring procedure, can be readily dosed to persons lying on their side in bed, and can be retained sufficiently at a site in oral cavity or throat where the pharmaceutical component therein can be absorbed or at a site to be therapeutically treated. Thus, the medicinal composition of the invention is preferable for administration to patients with deglutition disorder or persons with swallowing difficulty.

CLAIMS

1. An oral medicinal composition comprising an active ingredient and at least one foaming agent, which is ejected from a foam-developing device to be prepared into foam.

2. An oral medicinal composition according to claim 1, where the foaming agent is at least one selected from the group consisting of polyethylene glycol, saponin, sucrose esters of fatty acids, polyoxyl stearate, polyoxyethylene hydrogenated castor oil, polyoxyethylene polyoxypropylene glycol, sorbitan sesquioleate, sorbitan trioleate, sorbitan monostearate, sorbitan monopalmitate, sorbitan monolaurate, polysorbate, glyceryl monostearate, sodium lauryl sulfate and lauromacrogol.

3. An oral medicinal composition according to claim 2, where the foaming agent is at least one selected from the group consisting of polysorbate, polyethylene glycol and sodium lauryl sulfate.

4. An oral medicinal composition according to claim 3, where the foaming agent is a mixture of polyethylene glycol and polysorbate or a mixture of polyethylene glycol and sodium lauryl sulfate.

5. A method for administering an oral medicinal composition, which comprises ejecting an oral medicinal composition comprising an active ingredient and at least one foaming agent from a foam-developing device to prepare the oral medicinal composition into foam for administration.

6. A method for administering an oral medicinal composition according to claim 5, where the foaming agent is at least one selected from the group consisting of polyethylene glycol, saponin, sucrose esters of fatty acids, polyoxyl stearate, polyoxyethylene hydrogenated castor oil, polyoxyethylene polyoxypropylene glycol, sorbitan sesquioleate, sorbitan trioleate, sorbitan monostearate, sorbitan monopalmitate, sorbitan monolaurate, polysorbate, glyceryl monostearate, sodium lauryl sulfate and lauromacrogol.

7. A method for administering an oral medicinal composition according to claim 6, where the foaming agent is at least one selected from the group consisting of polysorbate, polyethylene glycol and sodium lauryl sulfate.

8. A method for administering an oral medicinal composition according to claim 7, where the foaming agent is a mixture of polyethylene glycol and polysorbate or a mixture of polyethylene glycol and sodium lauryl sulfate.

ABSTRACT

The present invention relates to an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is ejected from a foam-developing device to be prepared into foam, and a method for administering an oral medicinal composition comprising an active ingredient and at least one foaming agent, which is ejected from a foam-developing device to prepare the oral medicinal composition into foam for administration, the composition being preferably applicable to patients with deglutition disorder or persons with swallowing difficulty.

Express Mail Label No.

Docket No.
SDF 02-8

Declaration and Power of Attorney For Patent Application

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled
Medicinal Compositions For Oral Use

the specification of which

(check one)

☐ is attached hereto.

☒ was filed on **February 28, 2002** as United States Application No. or PCT International Application Number 10/069,780

and was amended on _____
(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
PCT/JP00/05677	**Japan**	**24/August/2000**	☐
(Number)	(Country)	(Day/Month/Year Filed)	
250837/1999	**Japan**	**3/September/1999**	☐
(Number)	(Country)	(Day/Month/Year Filed)	
			☐
(Number)	(Country)	(Day/Month/Year Filed)	

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below

(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U. S. C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C. F. R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(list name and registration number)*

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Fifth inventor's signature

Date

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Full name of sixth inventor, if any

Sixth inventor's signature

Date

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